

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (original) A polypeptide comprising more than two ligand binding domains of a cytokine receptor wherein said domains are linked by a linker molecule and wherein the linker molecule comprises at least one proteolytic cleavage site.

2. (original) A polypeptide according to claim 1 wherein said cleavage site is sensitive to a serum protease.

3. (original) A polypeptide according to claim 2 wherein the serum protease is thrombin.

4. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein said cleavage site comprises the amino acid sequence LVPRGS (SEQ ID:1), or a variant thereof.

5. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein said cleavage site comprises the amino acid sequence SGGGG (SEQ ID:2), or a variant thereof.

6. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein said cleavage site comprises the amino acid sequence PGISGGGGG (SEQ ID:3).

7. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 4 wherein said cleavage site comprises the amino acid sequence: LVPRGSPGISGGGGG (SEQ ID:4), or a variant thereof.

8. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 5 wherein said cleavage site comprises ~~at least~~ a center and

two copies of the amino acid sequence SGGGG, or a variant thereof, which flank the center of said cleavage site.

9. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein said polypeptide comprises at least four ligand binding domains.

10. (currently amended) A polypeptide according to claim 9 wherein said polypeptide ~~[[has]]~~ comprises 4, 6, 8, 10, or 12 ligand binding domains.

11. (currently amended) A polypeptide according to ~~any of the preceding claims 1 to 8~~ claim 1 wherein said polypeptide ~~[[has]]~~ comprises 3, 4, 5, 6, 7, 8, 9, or 10 ligand binding domains.

12. (currently amended) A polypeptide according to ~~any of the preceding claims 1 to 9~~ claim 9 wherein said polypeptide ~~[[has]]~~ comprises greater than 10 ligand binding domains.

13. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein said polypeptide is an antagonist to said cytokine.

14. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein said polypeptide is an agonist to said cytokine.

15. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein said cytokine receptor ligand binding domain is ~~selected from the ligand binding domains~~ domain of ~~the cytokines~~ a cytokine selected from the group consisting of: growth hormone; leptin; erythropoietin; prolactin; interleukins (IL), IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, ~~[[IL-11;]]~~ IL-11, the p35 subunit of IL-12, IL-13, IL-15; granulocyte colony stimulating factor ~~[[G-CSF;]]~~ (G-CSF), granulocyte macrophage colony stimulating factor (GM-CSF); ciliary neurotrophic factor ~~(CNTF)~~ (CNTF), cardiotrophin-1 ~~[[CT-1;]]~~ (CT-1), leukaemia inhibitory factor ~~(LIF)~~ (LIF), oncostatin M ~~(OSM)~~ (OSM), interferon, IFN $\alpha$  and IFN $\gamma$ .

16. (original) A polypeptide according to claim 15 wherein the binding domain is the ligand binding domain of growth hormone.

17. (original) A polypeptide according to claim 16 wherein the binding domain is the ligand binding domain of leptin.

18. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein the linker is a polypeptide which comprises from 5 to 50 amino acid residues.

19. (original) A polypeptide according to claim 18 wherein the linker comprises from 5 to 30 amino acid residues.

20. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein the linker comprises at least one copy of the peptide ~~Gly Gly Gly Gly Ser~~ GGGGS.

21. (currently amended) A polypeptide according to claim 20 wherein the linker is 5 amino acids in length and consists of one copy of the ~~(Gly4Ser)~~ linker GGGGS (the Gly4Ser linker).

22. (currently amended) A polypeptide according to claim 20 wherein the linker is 10 amino acids in length and consists of two copies of the ~~(Gly4Ser)~~<sup>2</sup> Gly4Ser linker.

23. (currently amended) A polypeptide according to claim 20 wherein the linker is 15 amino acids in length and consists of three copies of the ~~(Gly4Ser)~~ Gly4Ser linker.

24. (currently amended) A polypeptide according to claim 20 wherein the linker is 20 amino acids in length and consists of 4 copies of the ~~(Gly4Ser)~~<sup>4</sup> Gly4Ser linker.

25. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 wherein the polypeptide is a fusion protein comprising inframe translational fusions of ligand binding domains.

26. (currently amended) A polypeptide according to ~~any of the preceding claims~~ claim 1 comprising chemical crosslinkers wherein the chemical crosslinkers serve to link the ligand binding domains.

27. (currently amended) A polypeptide according to claim 26 wherein the chemical crosslinker comprises a homo-bifunctional crosslinker selected from the group consisting ~~[[of;]]~~ of disuccinimidyl-suberimidate-dihydrochloride; dimethyl-adipimidate-dihydrochloride; and 1,5,-2,4 dinitrobenzene.

28. (currently amended) A polypeptide according to claim 26 or claim 27 wherein the crosslinker comprises a hetero-bifunctional crosslinker selected from the group consisting ~~[[of;]]~~ of N-hydroxysuccinimidyl 2, 3-dibromopropionate; 1-ethyl-3-[3-dimethylaminopropyl] carbodiimide hydrochloride; and succinimidyl 4-[n-maleimidomethyl]-cyclohexane-1-carboxylate.

29. (currently amended) A nucleic acid molecule comprising a nucleic acid sequence which encodes a polypeptide according to ~~any of the preceding claims~~ claim 1.

30. (currently amended) A nucleic acid molecule comprising the sequence selected from the group consisting of:

- (i) the sequence represented by ~~[[Figs]]~~ Fig. 4 or 6;
- (ii) a sequence which hybridises to the sequence of (i) above and which has cytokine receptor modulating activity; and
- (iii) a sequence which is degenerate as a result of the genetic code to the sequences defined in (i) and (ii) above.

31. (currently amended) A nucleic acid molecule which hybridises under stringent hybridisation conditions to the sequences represented in ~~[[Figs]]~~ Fig. 4 or 6.

32. (currently amended) A polypeptide encoded by the nucleic acid molecule according to ~~any of claims 29 to 31~~ claim 29.

33. (original) A polypeptide according to claim 32 wherein said polypeptide is modified by deletion, addition, and/or substitution of at least one amino acid residue and said modification enhances the antagonistic or agonistic effects of said polypeptide with respect to the inhibition or activation of receptor mediated cell signalling.

34. (currently amended) A vector ~~including a DNA molecule wherein said DNA molecule encodes a polypeptide according to any of claims 1 to 28, 32 or 33~~ comprising the nucleic acid molecule of claim 29.

35. (original) A vector according to claim 34 wherein said vector is an expression vector adapted for prokaryotic or eukaryotic gene expression.

36. (currently amended) A vector according to claim 34 ~~or 35~~ wherein said vector further encodes, ~~and thus said recombinant polypeptide is provided with,~~ a secretion signal linked to the polypeptide to facilitate purification of ~~[[said]]~~ the polypeptide.

37. (currently amended) A method to prepare a polypeptide according to ~~any of claims 1 to 28, 32 or 33~~ claim 1, the method comprising;

(i) growing a cell transformed or transfected with a nucleic acid of ~~any of claims 29 to 31 or a vector of claims 34 to 36~~ claim 29 in conditions conducive to the manufacture of said polypeptide; and

(ii) purifying said polypeptide from said cell, or its growth environment.

38. (currently amended) A cell transformed/transfected with the vector of ~~claims 34 to 36~~ or the nucleic acid of ~~claims 29 to 31~~ claim 29.

39-42. (cancelled)

43. (new) A pharmaceutical composition comprising the polypeptide according to claim 1, and a pharmaceutically acceptable carrier, excipient, or a diluent.

44. (new) A pharmaceutical composition comprising the nucleic acid molecule of claim 29 and a pharmaceutically acceptable excipient.

45. (new) A method for treating a disease selected from the group consisting of: acromegaly; gigantism; GH deficiency; Turners syndrome; renal failure; osteoporosis; diabetes mellitus; cancer; obesity; insulin resistance; hyperlipidaemia; hypertension; anaemia; an autoimmune disease; an infectious disease; an inflammatory disorder, and rheumatoid arthritis, wherein said method comprising administering to a patient in need thereof a pharmaceutical composition according to claim 43.

46. (new) A method for treating a disease selected from the group consisting of: acromegaly; gigantism; GH deficiency; Turners syndrome; renal failure; osteoporosis; diabetes mellitus; cancer; obesity; insulin resistance; hyperlipidaemia; hypertension; anaemia; an autoimmune disease; an infectious disease; an inflammatory disorder, and rheumatoid arthritis, wherein said method comprising administering to a patient in need thereof a pharmaceutical composition according to claim 44.